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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,911	07/07/2005	Peter D Senter	SGEN-0051/1000-00212US	7034

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EXAMINER	
BRADLEY, CHRISTINA	

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
03/20/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,911	SENTER ET AL.	
	Examiner	Art Unit	
	Christina Marchetti Bradley	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 7, 9, 17, 18, 20, 21, 27, 30, 54, 56, 63, 66, 77, 79, 111, 119, 121, 124-128 and 130-132* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1,7,9,17-30,44-46,48,49,52,54,56,59,63,66,77,79,100,104,111,119,121,122 and 124-132.
Continuation of Disposition of Claims: Claims withdrawn from consideration are 19,22-26,28,29,44-46,48,49,52,59,100,104,122 and 129.

DETAILED ACTION

Election/Restrictions

1. Claims 1, 7, 9, 17-30, 44-46, 48, 49, 52, 54, 56, 59, 63, 66, 77, 79, 100, 104, 111, 119, 121, 122 and 124-132 are pending. Claims 19, 22-26, 28, 29, 44-46, 48, 49, 52, 59, 100, 104, 122 and 129 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election of the species depicted in claim 79 wherein L is an anti-CD30 antibody and p is 4 was made **without** traverse in the reply filed on 12/19/2007. A prior art rejection under 35 U.S.C. 102(a) is made over this species. The prior art cited in this rejection also teaches the species of claim 77, which also reads on claims 30 and 56. Because a prior art rejection is made, the search was not extended in accordance with MPEP § 803.02.

Specification

2. The objection to the abstract for its content and to the specification for the use of the trademark Chromatotron is withdrawn in light of the amendment filed 07/30/2008.

Claim Rejections - 35 USC § 112

3. The rejection of claims 1, 2, 7, 9, 17-21, 27, 54, 63, 66, 79, 111-121 and 123 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement with respect to the claim term "solvate" is withdrawn in light of the amendment to the claims filed 07/30/2008.

4. The rejection of claims 1, 2, 7, 9, 17-21, 27, 54, 63, 66, 79, 111-121 and 123 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement with respect to the claim term "solvate" is withdrawn in light of the amendment to the claims filed 07/30/2008.

5. The rejection of claims 111-119 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is withdrawn in light of the amendment to the claims filed 07/30/2008.

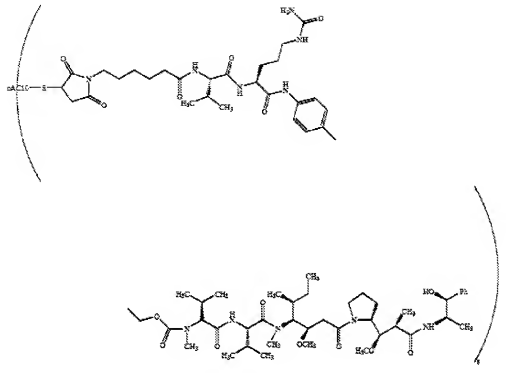
6. The rejection of claims 1, 2, 7, 17-19, 20, 21, 27, 111-121 and 123 under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements is withdrawn in light of the amendment to the claims filed 07/30/2008.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

8. The rejection of claims 1, 2, 7, 9, 17-21, 27, 54, 63, 66, 79, 111, 120, 121 and 123 under 35 U.S.C. 102(e) as being anticipated by Law *et al.* (U.S. Publication No. 2005/0123536, Application No. 10/496,628, filed 11/20/2002) is withdrawn. Application No. 10/496,628 claims priority to provisional Application No. 60/331,750 filed 11/20/2001. Provisional Application No. 60/331,750 does not disclose the species:

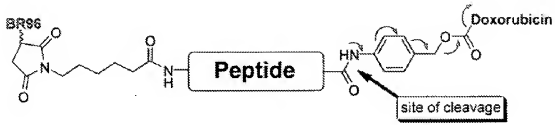


Therefore, the reference does not qualify as prior art under 35 U.S.C. 102(e) over the instant application which has an earliest effective filing date of 07/31/2002.

9. In light of the response to the request for information filed 01/08/2009, the following new grounds of rejection is made.

10. Claims 1, 7, 9, 17, 18, 20, 21, 27, 30, 54, 56, 63, 66, 77, 79, 111, 119, 121, 124-128 and 130-132 are rejected under 35 U.S.C. 102(a) as being anticipated by Toki *et al.* Toki *et al.* made an oral presentation at the 223rd ACS National Meeting in Orlando, FL on April 7-11 titled: "Cures and regressions of established tumor xenografts with monoclonal antibody auristatin" . A copy of the presentation was provided by Applicant in the response filed 01/08/2009.

The slides disclose the antibody-drug conjugate



wherein the peptide is Phe-Lys or Val-Cit, the antibody is BR96 and the drug is doxorubicin and the number of drug molecules per antibody molecule is 8 (p=8). The slides also disclose by name only the antibody-drug conjugates cBR96-phelys-MMAE, cAC10-phelys-MMAE, cBR96-valcit-MMAE, and cAC10-valcit-MMAE. Based on the structure for the antibody-drug conjugate with doxorubicin, and the compound names cBR96-phelys-MMAE, cAC10-phelys-MMAE, cBR96-valcit-MMAE, and cAC10-valcit-MMAE, the skilled artisan could readily envisage the antibody-drug conjugates of the instant claims. For cBR96-phelys-MMAE, the ligand is the antibody that binds to the cBR96 antigen, the dipeptide linker is Phe-Lys, the self-immolative spacer is p-amino benzyl carbamate and the drug is MMAE, which anticipates the structure in instant claim 1, 7, 9, 17, 18, 20, 21, 27, 29, 30, 56, 63, 77, 111, 119, 128 and 130-132. For cAC10-phelys-MMAE, the ligand is the antibody that binds to the cAC10 antigen, the dipeptide linker is Phe-Lys, the self-immolative spacer is p-amino benzyl carbamate and the drug is MMAE, which anticipates the structure in instant claim 1, 7, 9, 17, 18, 20, 21, 27, 29, 30, 56, 63, 77, 111, 119, 128 and 130-132. For cBR96-valcit-MMAE, the ligand is the antibody that binds to the cBR96 antigen, the dipeptide linker is Val-Cit, the self-immolative spacer is p-amino benzyl carbamate and the drug is MMAE, which anticipates the structure in instant claim 1, 7, 9, 17, 18, 20, 21, 27, 29, 54, 63, 66, 79, 111, 119, 121, 124-128 and 130-132. For cAC10-valcit-MMAE, the ligand is the antibody that binds to the cAC10 antigen, the dipeptide linker is Val-

Cit, the self-immolative spacer is p-amino benzyl carbamate and the drug is MMAE, which anticipates the structure in instant claim 1, 7, 9, 17, 18, 20, 21, 27, 29, 54, 63, 66, 79, 111, 119, 121, 124-128 and 130-132.

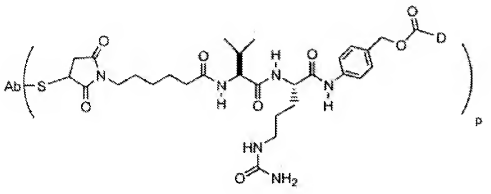
Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

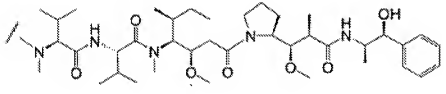
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 1, 7, 9, 17, 18, 20, 21, 27, 54, 63, 66, 79, 111, 119, 121, 124-127, and 130-132 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-36 and 40-89 of copending Application No. 11/833,959. Although the conflicting claims are not identical, they are not patentably distinct from each other. Claim 68 claims an antibody-drug conjugate compound or a pharmaceutically acceptable salt or solvate thereof



wherein D is



Wherein p is 1 to 20. This antibody-drug conjugate anticipates claims 1, 7, 9, 17, 20, 21, 27, 54, 63, 119, 121, 127, 131 and 132 of the instant application. With respect to claim 18, claim 76 of copending Application No. 11/833,959 states that the antibody is a monoclonal antibody. With respect to claims 66 and 130, the skilled artisan can readily envisage p equal to 1 to 8. With respect to claims 79 and 126, claim 76 of copending Application No. 11/833,959 states that the antibody is a monoclonal antibody and the skilled artisan can readily envisage p equal to 1 to 8. With respect to claims 111, 124 and 125, claim 90 of copending Application No. 11/833,959 recites a pharmaceutical composition of the antibody-drug conjugate. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

13. Claims 1, 7, 9, 17, 18, 20, 21, 27, 29, 30, 54, 56, 63, 66, 77, 79, 111, 119, 121, 124-128 and 130-132 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-19 of copending Application No. 12/016,978 in view of Dubowchik *et al.* ("Cathepsin B-Sensitive Dipeptide Prodrugs. 2. Models Of Anticancer Drugs Paclitaxel (Taxol®), Mitomycin C And Doxorubicin," *Bioorganic & Medicinal Chemistry Letters*, **1998**, *8*, 3347-52) and Blatter *et al.* (US 4,764,368). Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claims 13 and 14 of copending Application No. 12/016,978 recite an antibody-drug conjugate in which the antibody is conjugated to MMAE by a linker of formula -Ta-Ww-Yy wherein T is a stretcher, a is 0 or 1, W is an amino acid, w is an integer ranging from 2 to 12, Y is a spacer and y is 0, 1 or 2.

The conflicting claims do not recite the spacer Aa-Ww-Yy wherein Y is a self-immolative spacer of the instant claims.

Dubowchik *et al.* teach cathepsin B-sensitive dipeptide prodrugs wherein the cytotoxic anticancer drugs doxorubicin, paclitaxel and mitomycin C are conjugated to a dipeptide (Lys, Arg or Cit at P1 and Phe or Val at P2) and a self-immolative spacer p-aminobenzylcarbonyl. Dubowchik *et al.* teach that the "compounds release free drug in the presence of cathepsin B and in a rat liver lysosome preparation with half-lives that, in combination with their excellent human plasma stability, make them good candidates to be used as extracellularly-stable drug-linker combinations for targeted drug therapy." (p. 3351)

Blatter *et al.* teach heterobifunctional reagents such as 6-maleimidocaproic acid for use as crosslinkers in drug-antibody conjugates.

It would have been obvious to one of ordinary skill in the art to use the cathepsin B-sensitive dipeptide and self-immolative spacer p-aminobenzylcarbonyl linker taught by Dubowchik *et al.* in combination with the 6-maleimidocaproic acid taught by Blatter *et al.* as the linker in the antibody-drug conjugate recited in claims 13 and 14 of copending Application No. 12/016,978. The skilled artisan would have been motivated to do so given that Dubowchik *et al.* teach that the linker is stable in human plasma and is cleaved in lysosomes and that Blatter *et al.* demonstrate that the 6-maleimidocaproic acid group can be used to couple a drug-linker conjugate to an antibody (Fig. 2). There would have been a reasonable expectation of success given that Dubowchik *et al.* demonstrate that the linker can be conjugated to an amino functional group of a drug and that MMAE contains a reactive amino group. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

14. The rejection of claims 1, 7, 9, 17-21, 27, 54, 63, 66, 79, 111, 121, 131 and 132 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-44 and 48-103 of copending Application No. 11/833,954 is withdrawn in light of the amendments filed 08/29/2008 and 07/30/2008.

15. The rejection of claims 112, 113 and 116 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-54 of copending Application No. 11/833,961 is withdrawn because claims 112, 113 and 116 are cancelled.

16. The rejection of claims 112, 113 and 116 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-54 of copending Application No. 11/833,964 is withdrawn because claims 112, 113 and 116 are cancelled.

17. The rejection of claims 112, 113 and 116 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 8 and 9 of copending Application No. 10/558,811 is withdrawn because claims 112, 113 and 116 are cancelled.

18. The rejection of claims 1, 2, 7, 9, 17-21, 27, 54, 63, 66, 79, 111, 120, and 121 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 74-94, 109 and 222-235 of copending Application No. 10/983,340 is withdrawn in light of the amendments filed 08/29/2008 and 07/30/2008.

19. The rejection of claims 1, 2, 7, 9, 17-21, 27, 54, 63, 66, 79, 111-114, 116, 117, and 119-121 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-18 of copending Application No. 11/667,437 is withdrawn in light of the amendments filed 08/29/2008 and 07/30/2008.

20. The rejection of claims 1, 2, 7, 9, 17-21, 27, 54, 63, 66, 79, and 111-121 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 53-99 of copending Application No. 11/994,459 is withdrawn in light of the amendments filed 08/29/2008 and 07/30/2008.

21. The rejection of claims 1, 2, 7, 9, 17-21, 27, 54, 63, 66, 79, and 111-121 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 28-73 of copending Application No. 11/994,809 is withdrawn in light of the amendments filed 08/29/2008 and 07/30/2008.

22. The rejection of claims 112, 113 and 116 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-40 of copending Application No. 11/677,029 is withdrawn because the claims are cancelled.

Conclusion

23. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Marchetti Bradley whose telephone number is (571)272-9044. The examiner can normally be reached on Monday-Thursday, 8:30 A.M. to 4:00 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Cecilia Tsang/
Supervisory Patent Examiner, Art Unit 1654

/Christina Marchetti Bradley/
Examiner, Art Unit 1654